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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/665,976	09/20/2000	Lawrence W. Stanton	SCIOS.014A	8472

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EXAMINER	
SOUAYA, JEHANNE E	

ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 11/13/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/665,976	STANTON ET AL.	
	Examiner	Art Unit	
	Jehanne Souaya Sitton	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *07 August 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *31* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *31* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *8/2003*.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Currently, claim 31 is pending in the instant application. All the amendments and arguments have been thoroughly reviewed but are deemed insufficient to place this application in condition for allowance. Any rejections not reiterated are hereby withdrawn. The following rejections are either newly applied or are reiterated. They constitute the complete set being presently applied to the instant Application. Response to Applicant's arguments follow. This action is FINAL.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Maintained Rejections

Claim Rejections - 35 USC § 101

3. Claim 31 is rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific or substantial asserted utility or a well established utility.

The claimed nucleic acids are not supported by a specific asserted utility because the disclosed uses of the nucleic acids are not specific and are generally applicable to any nucleic acid. The specification teaches that the invention is based on the identification of a gene that is differentially expressed in the left ventricle of the rat Myocardial infarction model, in the rat Cardiac Hypertrophy Model, and in the mouse Viral Myocarditis model (p. 20, lines 9-11). Claim 31 is directed to the cDNA sequence of that gene. The specification states that the nucleic

acids of the invention, and particularly SEQ ID NO 2 can be used to design specific probes and primers, can be used in detection, diagnostic, prognostic methods, vector constructs, antibody constructs, etc (p. 42-48). These are non-specific uses that are applicable to nucleic acids in general and not particular or specific to the nucleic acid being claimed.

Further, the claimed nucleic acids are not supported by a substantial utility because no substantial utility has been established for the claimed subject matter. The specification states that when characterization of the differentially expressed genes indicate that modulation of the gene's expression or the gene product's activity can inhibit or treat a disease, specifically cardiac, kidney, or inflammatory diseases, the differentially expressed gene or it's gene product becomes a potential drug candidate or a target for developing a drug candidate for the treatment of a cardiac, kidney or inflammatory disease, or may be used as a diagnostic. However, the specification has not taught the activity of the polypeptide encoded by SEQ ID NO 2, nor has the specification demonstrated that the modulation of the expression of SEQ ID NO 2 can be used to inhibit or treat any kidney, inflammatory, or cardiac disease, including viral myocarditis, cardiac hypertrophy, or myocardial infarction. The need for such research clearly indicates that the nucleic acid or the protein it encodes is not disclosed as to a currently available or substantial utility. A starting material that can only be used to produce a final product does not have substantial asserted utility in those instances where the final product is not supported by a specific and substantial utility. Further, a starting material does not have substantial utility when further experimentation must be conducted to determine the use for that starting material. The research contemplated by applicant(s) to characterize potential protein products, and determine therapeutic and diagnostic uses does not constitute a specific and substantial utility. Identifying

and studying the properties of a nucleic acid or protein itself or the mechanisms in which such are involved does not define a "real world" context or use. Similarly, the other listed and asserted utilities as summarized above or in the instant specification are neither substantial nor specific due to being generic in nature and applicable to a myriad of such compounds. Note, because the claimed invention is not supported by a specific and substantial asserted utility for the reasons set forth above, credibility of the utility has not been assessed. Neither the specification as filed nor any art of record discloses or suggests any property or activity for the nucleic acid and/or protein compound(s) such that another non-asserted utility would be well established for the compounds.

It is noted that the specification asserts that the differentially expressed nucleic acids can be used as a diagnostic. This assertion has been thoroughly reviewed, however the teachings of the specification do not support how one of skill in the art would use the claimed nucleic acid as a diagnostic. Firstly, it is noted that the specification teaches that in vivo experimentation revealed that in the rat myocardial infarction model and the rat cardiac hypertrophy model, the gene corresponding to SEQ ID NO 2 was under expressed by about 1.8 fold and 2.5 fold, respectively. This expression pattern, however, does not appear to be diagnostic of cardiac diseases in general as the specification teaches that in vivo, the gene corresponding to SEQ ID NO 2 was over expressed in the mouse viral myocarditis model (See p. 65, lines 15-24). Furthermore, the specification fails to teach corroborative evidence for such *in vivo* expression patterns. The specification teaches that in *in vitro* experiments, rat cardiac myocytes were treated with various growth factors and cytokines known to induce cardiac hypertrophy (see p. 72, lines 7-9). However, while SEQ ID NO 2 was under expressed in the in vivo rat cardiac hypertrophy model, it was over expressed in cardiac myocytes cells where cardiac hypertrophy

was induced (see p. 74, and figure 4). Therefore, given the results in the specification, the skilled artisan would not be able to identify a specific cardiac disease based on detection of either over expression or under expression of SEQ ID NO 2. Further experimentation would be required of the skilled artisan to reasonably confirm a real world context of use for the claimed nucleic acids.

The response traverses the rejection. The response asserts that differential expression of the claimed sequence was reasonably correlated to three specific cardiac diseases, myocardial infaction, cardiac hypertrophy, and viral myocarditis. The response asserts that because the specification discloses a correlation among differential expression levels of SEQ ID NO 2 with a variety of diseases, the claims are supported by a specific utility. The response also asserts that the subject matter has a substantial utility because the claimed subject has is useful in diagnosing various cardiac disease states. These arguments have been thoroughly reviewed but were found unpersuasive. While the specification shows differential expression with regard to SEQ ID NO: 2 in different types of cardiac diseases, this expression pattern is not correlative with regard to cardiac diseases in general or even between the same cardiac disease state in in vivo vs in vitro models. Thus, the mere fact that SEQ ID NO: 2 shows differential expression in cardiac diseases, such is not considered substantial because cardiac diseases can involve a large number of diseases that are not necessarily related to each other, and it is unclear whether over or under expression of SEQ ID NO: 2 is associated with such. For example, the specification teaches that in *in vitro* experiments, rat cardiac myocytes were treated with various growth factors and cytokines known to induce cardiac hypertrophy (see p. 72, lines 7-9). However, while SEQ ID NO 2 was under expressed in the in vivo rat cardiac hypertrophy model, it was over expressed in cardiac myocytes cells where cardiac hypertrophy was induced (see p. 74, and figure 4).

Therefore, the differential expression exhibited by the specification is unclear as to whether cardiac hypertrophy is correlated with under or over expression of SEQ ID NO: 2. The skilled artisan would have to perform further experimentation to determine how to use SEQ ID NO: 2 to diagnose cardiac hypertrophy. Further, although the in vivo cardiac models indicate that differential expression of SEQ ID NO: 2 could be associated with different cardiac disease states, the conflicting in vitro data presented by the specification, indicates that further experimentation must be conducted to determine if and how the differential expression of SEQ ID NO: 2 is correlated to different disease states. The rejection is maintained.

Claim Rejections - 35 USC § 112

4. Claim 31 is also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific or substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

The claim is drawn to an isolated nucleic acid comprising the sequence of SEQ ID NO 2, or the portion of SEQ ID NO 2 that codes SEQ ID NO 1.

While the specification asserts that the differentially expressed nucleic acids can be used as a diagnostic. This assertion has been thoroughly reviewed, however the teachings of the specification do not support how one of skill in the art would use the claimed nucleic acid as a diagnostic. Firstly, it is noted that the specification teaches that in vivo experimentation revealed that in the rat myocardial infarction model and the rat cardiac hypertrophy model, the gene

corresponding to SEQ ID NO 2 was under expressed by about 1.8 fold and 2.5 fold, respectively. This expression pattern, however, does not appear to diagnostic of cardiac diseases in general as the specification teaches that in vivo, the gene corresponding to SEQ ID NO 2 was over expressed in the mouse viral myocarditis model (See p. 65, lines 15-24). Furthermore, the specification fails to teach corroborative evidence for such *in vivo* expression patterns. The specification teaches that in *in vitro* experiments, rat cardiac myocytes were treated with various growth factors and cytokines known to induce cardiac hypertrophy (see p. 72, lines 7-9). However, while SEQ ID NO 2 was under expressed in the in vivo rat cardiac hypertrophy model, it was over expressed in cardiac myocytes cells where cardiac hypertrophy was induced (see p. 74, and figure 4). The specification provides no guidance as to the differences in expression pattern of SEQ ID NO 2 with regard to these cardiac diseases. Therefore, given the results in the specification, the skilled artisan would not be able to identify a specific cardiac disease based on detection of either over expression or under expression of SEQ ID NO 2. Further empirical experimentation would be required for the skilled artisan to determine a use for the claimed nucleic acid. This experimentation would largely consist of trial and error analysis, as the results in the specification demonstrate the unpredictability of the use for SEQ ID NO 2 as a diagnostic. The art does not provide any teaching to overcome the unpredictability taught in the specification. Therefore, the experimentation required of the skilled artisan to determine how to use the claimed nucleic acid is considered undue.

The response traverses the rejection. The response asserts that the claimed subject matter functions as a diagnostic and serves the specific and substantial purpose of allowing a clinician to make an initial assessment regarding whether a patient is suffering from a cardiac disease such

as infarction, hypertrophy, or viral myocarditis. This argument has been thoroughly reviewed but was found unpersuasive because given the conflicting evidence in the specification with regard to different expression levels with regard to SEQ ID NO: 2, not only between different cardiac disease, but also between in vivo and in vitro experiments with the same cardiac disease, a clinician would not be capable of determining whether a patient was suffering from cardiac hypertrophy or viral myocarditis or myocardial infarction solely based on the differential expression of SEQ ID NO: 2. Further, unpredictable experimentation, as evidenced by the conflicting data in the specification, would be required to determine how to use SEQ ID NO: 2 to diagnose cardiac hypertrophy, or viral myocarditis, or infarction. The unpredictability of the outcome of such experimentation is what renders it undue. The Mason et al reference has been thoroughly reviewed but was found unpersuasive as it does not contain any evidence or discussion as to how to use expression levels of SEQ ID NO: 2 to diagnose cardiac hypertrophy or viral myocarditis or myocardial infarction. The rejection is maintained.

Conclusion

5. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37

CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

6. No claim is allowable.

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Jehanne Sitton whose telephone number is (703) 308-6565. The examiner can normally be reached Monday-Thursday from 8:00 AM to 5:00 PM and on alternate Fridays.

Note: The examiner's name has changed from Jehanne Souaya to Jehanne Sitton. All future correspondence to the examiner should reflect the change in name. It is also noted that after January 12, 2004, the examiner will be located at the new USPTO campus and will be reachable at telephone number (571) 272-0752.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached on (703) 308-1152. The fax phone number for this Group is (703) 872-9306.

Any inquiry of a general nature should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Jehanne Souaya Sitton

Jehanne (Souaya) Sitton
Primary Examiner
Art Unit 1634
11/10/03